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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/323,738	06/01/99	OSBORNE W	P-UW-3570

023601
CAMPBELL & FLORES LLP
4370 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO CA 92122

HM12/0919

EXAMINER	
ENGLISH, S	
ART UNIT	**PAPER NUMBER**
1644	12

DATE MAILED: 09/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/323,738	Osborne et al.
Examiner	**Art Unit**
G. R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 2, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above, claim(s) *1-16 and 40* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-39* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Dr. Gerald R. Ewoldt, Group Art Unit 1644.

2. In view of response, filed 7/02/01, all previous rejections have been withdrawn.

3. The following are New Grounds for Rejection.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 17-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of treating diabetes or forestalling a clinical symptom indicative of diabetes comprising implanting into an individual smooth muscle cells comprising a polyfluoroethylene prosthetic graft transfected with the vector/plasmid LhI*TgFuSN, does not reasonably provide enablement for:

a method of treating diabetes or forestalling a clinical symptom indicative of diabetes comprising implanting into an individual cells:

A) coexpressing proinsulin containing a proinsulin cleavage site,

B) coexpressing a glucose-regulated protease,

C) comprising a proinsulin cleavage site consisting of SEQ ID NO:7 .

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the breadth of the compositions encompassed by the claims.

Note that the specification provides a single *in vivo* example consisting of the expression of a single nucleic acid construct in a single cell type demonstrating the efficacy of the claimed method. The pending claims, however, are generic in nature, encompassing any cell type that might express any proinsulin comprising any protease cleavage site that might be cleaved by any protease expressed under a glucose-regulated promoter. The specification is insufficient to support such generic claims.

Specifically, as claimed, the method would encompass the use of transfected β islet cells which are well known in the art to comprise antigens targeting said cells for destruction in a diabetic individual. As such, the claimed method could not function employing said cells (see Janeway et al., 1994).

Regarding "proinsulin containing a proinsulin cleavage site," proinsulin is a well-known molecule, see for example Stryer (1981), known to require two cleavages to become insulin. Thus, the recited method can not function as claimed because insulin can not be derived from proinsulin after a single cleavage. Applicant's attempt to redefine "proinsulin" as a recombinant molecule capable of becoming insulin after a single cleavage is improper and must be considered an attempt to redefine "proinsulin" in a way that would be repugnant to the usual meaning of the term.

Regarding "coexpressing a glucose-regulated protease," the single working example of the specification discloses the use of a single protease, furin, while the specification lists a number of additional proteases, including PC2 and PC3. The prior art however, teaches that the proteases are not interchangeable. See, for example, Smeekens et al. (1992, IDS) which teaches that while furin is capable of converting proinsulin to insulin, PC2 alone is not. Thus, the recited method can not function through the use of any "glucose-regulated protease" as claimed.

Finally note that Claims 27 and 39 recite a protease cleavage site comprising SEQ ID NO:7. The single working example of the specification, however, discloses the use of a protease cleavage site comprising SEQ ID NO:8. Given the teachings of Smeekens et al. (above) teaching that insulin cleaving proteases are not interchangeable, as well as Groskreutz et al. (1994, IDS), which indicates that the furin consensus cleavage site comprises SEQ ID NO:8, the practice of the invention as claimed would be highly unpredictable.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of other than a single working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

6. Claims 28-30 and 32-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of a "hexoamine biosynthetic pathway enzyme," other than glutamine:fructose-6-phosphate amidotransferase. The specification discloses just the single species of the claimed genus, thus, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe said claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
September 17, 2001

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600